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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/520,169	04/27/2005	Andrew David Bacon	Q85454	9237

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EXAMINER	
CHEN, SHIN LIN	
ART UNIT	**PAPER NUMBER**
1632	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/520,169	BACON ET AL.	
	Examiner	Art Unit	
	Shin-Lin Chen	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 December 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13,16 and 25-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13, 16 and 25-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' amendment filed 12-26-07 has been entered. Claims 13, 16 and 25 have been amended. Claims 1-12, 15 and 17-24 have been canceled. Claims 27-30 have been added. Claims 13, 16 and 25-30 are pending and under consideration.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 13, 16 and 25-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicants' amendment filed 12-26-07 necessitates this new ground of rejection.

The phrase "said nucleic acid and said assistor protein associated together and associated with liposome" in amended claim 13 is vague and renders the claim indefinite. It is unclear what are "associated together" and what is "associated with" liposome. Claims 16 and 25-28 depend from claim 13.

The term "HA" in claim 29 is vague and renders the claim indefinite. The term "HA" is an abbreviation that can stand for various meanings. It is unclear what meaning is intended in the claim. Spelling out the term "HA" would be remedial. Claim 30 depends from claim 29.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 13, 16 and 25-28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicants' amendment filed 12-26-07 necessitates this new ground of rejection.

The phrase "the antigenic protein and the assistor protein are from an **infectious organism**" in amended claim 13 is considered new matter. The amendment filed 12-26-07 fails to point out where the support is for the phrase "the antigenic protein and the assistor protein are from an **infectious organism**". The term "organism" has a much broader scope than the term "microorganism". The specification fails to provide sufficient disclosure to support the phrase set forth above. Thus, the phrase set forth above is considered new matter. Claims 16 and 25-28 depend from claim 13.

The phrase "said nucleic acid and said assistor protein associated together and associated with liposome" in amended claim 13 is considered new matter. The amendment filed 12-26-07 fails to point out where the support is for the phrase "said nucleic acid and said assistor protein associated together and associated with liposome. The specification fails to provide sufficient disclosure to support the phrase set forth above. Thus, the phrase set forth above is considered new matter. Claims 16 and 25-28 depend from claim 13.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 13, 16, 25 and 26 remain rejected and newly added claims 27-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Craig, et al., 1997 (WO 97/28818) in view of Gregoriadis et al., 1999 (Methods, Vol. 19, p. 156-162, IDS) and is repeated for the reasons set forth in the preceding Official action mailed 6-22-07. Applicant's arguments filed 12-26-07 have been fully considered but they are not persuasive.

Applicants argue that the cited reference Craig does not appreciate the necessity of co-delivery of a shared epitope between the nucleic acid and the protein antigen and Craig only teaches the co-delivery as optional. Applicants further argue that Craig does not suggest that both the encoding nucleic acid and the protein be associated with the same liposomal delivery vehicle or comprise the same epitope (amendment, p. 5-6). This is not found persuasive because

of the reasons set forth in the preceding Official action mailed 6-22-07. Craig teaches administering a mixture to a mammal to elicit an immune response in said mammal, wherein the mixture includes a nucleic acid encoding a first epitope and a peptide containing a second epitope such that both of the nucleic acid and the second epitope are taken up by the antigen presenting cell of the mammal (e.g. abstract). Craig teaches that the first and second epitopes are preferably epitopes from the same antigen, and they may comprise the same immuno-dominant epitope from an infectious agents, such as the influenza virus (e.g. p. 4, lines 25-35, claims 24-30). Craig teaches "[i]n the simplest form, the peptide antigen and the nucleic acid encoded antigen described here are the same" (e.g. p. 17, lines 4-5). Craig teaches non-viral delivery means to deliver nucleic acid and an antigenic peptide or protein associated with nucleic acid to a mammal cell, wherein the non-viral delivery means include DNA/polycation complexes, self assembling virus like particles, and microsphere which are used for delivery of DNA or protein to cells, e.g. polyactide glycolide polymers, and **liposomes** (e.g. p. 12, lines 10-25). It is not necessary for Craig to teach only the claimed instant invention to make it obvious for one of ordinary skill in the art at the time of the invention. Maybe it is an option, however, Craig does teach combination of peptide antigen and nucleic acid encoding the same peptide antigen, and co-delivery of said nucleic acid and antigenic peptide or protein associated with said nucleic acid to a mammalian cell via liposome to stimulate an immune response in a mammal. In view of such teaching, it would be prima facie obvious to one of ordinary skill in the art to practice the instant invention as claimed.

Applicants argue that Craig teaches the nucleic acid encoded antigen is expressed only in professional antigen presenting cells (APCs) and the vehicle must be directed specifically to

APCs or the expression only occurs in APCs, and in the instant invention, the target moieties are excluded from claims 13 and 28 by "consisting essentially of" language. Applicants further argue that in the prophetic examples of Craig, only T cell response is expected (amendment, p. 6). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 6-22-07. It is "preferred" that the nucleic acid encoded antigen is expressed only in professional antigen-presenting cells (APC) (e.g. Craig, p. 7). It does not mean that this is the only option. There are other options that allow the nucleic acid encoded antigen to be expressed in any cells and it is not necessary that the liposome is directed only to APCs. Further, the claims read on generating an immune response in a mammal by administering to the mammal the claimed composition and the immune response "comprises" an antibody response. The claims do not exclude targeting the composition to APCs and the teaching of preferred embodiment by Craig that the nucleic acid encoded antigen is expressed in APCs still make it obvious for one of ordinary skill in the art to practice the instantly claimed invention. Craig teaches "it is desirable that the epitope (peptide, polypeptide, antigen) be as small as possible while still maintaining immunogenicity. Immunogenicity is indicated by the ability to elicit an immune response … and to induce a T cell response and an antibody response, and "'immune response' refers to either a cellular or a humoral immune response or to both a cellular and a humoral immune response" (e.g. p. 6). An example teaching T cell response is expected does not mean that T cell response is the only response expected by the method taught by Craig. Craig does anticipate immune response that includes T cell response and antibody response as discussed above. The "consisting essentially of" language does not necessarily exclude the target moieties and the claims fail to specifically mention what kind of target moiety is used and said target moiety is

excluded from the claimed method. The use of specific ligand to target a specific type of cell is only an option in the teachings of Craig. There are other options that only the nucleic acid and the peptide antigen are used for the method as taught by Craig.

Applicants argue that the in vivo working examples of Craig only teaches using a test protein, not an antigen, to be expressed in APCs and the expressed protein and the protein per se do not share an epitope in the in vitro working examples (e.g. amendment, p. 6-7). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 6-22-07 and the reasons set forth above. Although the working examples does not teach that the nucleic acid encoded protein and the peptide antigen share an epitope, it does not mean that it is not taught by Craig. Craig does teach combination of peptide antigen and nucleic acid encoding the same peptide antigen, and co-delivery of said nucleic acid and antigenic peptide or protein associated with said nucleic acid to a mammalian cell via liposome to stimulate an immune response in a mammal.

Applicants argue that teachings of Craig lack in vivo data and merely speculate extrapolation from limited and irrelevant in vitro work, which cannot show immune response, and there is no reasonable expectation of success in stimulating immune response. Applicants further argue that the instant invention shows combination of nucleic acids expression an antigen and the assistor protein containing a common epitope enhance the humoral response (amendment, p. 7-10). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 6-22-07 and the reasons set forth above. It should be noted that the claimed invention only requires generating immune response in a mammal. It was well known in the art an epitope of an antigen can stimulate immune response in vivo. Craig defines

the term "epitope" as it "refers to an immunogenic amino acid sequence. An epitope may refer to a minimum amino acid sequence of 6-8 amino acids (i.e., a peptide), which minimum sequence is immunogenic when removed from its natural context and is carried in an complex according to the invention as a peptide, or when transplanted into a heterologous polypeptide such that it retains its natural immunogenicity and thus is carried in a complex according to the invention as part of a polypeptide. An epitope also may refer to that portion of a natural polypeptide which is immunogenic, where the natural polypeptide containing the epitope is referred to as an antigen (Craig, p. 5). Thus, there is reasonable expectation of success that an immune response can be generated in vivo by using the method as taught by Craig. Further, there is nowhere in the claims that recite "enhanced" immune response as compared to a control by the instant invention. Even if the "enhanced" immune response is recited in the claims, Craig teaches that "the invention also encompasses the co-administration of two separate moieties, (i) nucleic acid and (ii) peptide antigen, as a mixture. It is believed that such co-administration will result in an increased ability of the APC to stimulate proliferation of autologous T cells compared to APC to which only DNA or protein/peptide antigen has been delivered (Craig, bridging pages 63 and 64).

Applicants argue that the in vivo example by Craig does not require that the nucleic acid encodes the same protein or a common epitope with the influenza nucleoprotein and since it is a prophetic example, it is not clear whether an enhanced immune response can be expected and no control is shown. Applicants argue that Craig teaches away from the invention because it merely requires nucleic acid and protein be delivered specifically to an antigen presenting cell

(amendment, p. 11-12). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 6-22-07 and the reasons set forth above.

Applicants argue that claim 27 is not suggested by Craig, even in combination with Gregoriadis, and this claim is not rejected over the art (amendment, p. 13). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 6-22-07 and the following reasons. Examiner is confused that why "this claim is not rejected over the art". Claim 27 is a newly added claim and the limitation of "said liposome lack phospholipid" has not been recited in the previous claims examined. It is unclear how "this claim is not rejected over the art". Gregoriadis teaches preparation of vaccine-containing liposomes by using polyethylene glycol 6000 (PEG 6000), which is not phospholipid. Although Craig does not specifically teach using liposome lacking phospholipid, however, Gregoriadis does teach preparing liposome lacking phospholipid. Thus, claim 27 is obvious to one of ordinary skill in the art at the time of the invention in view of the teachings of Craig and Gregoriadis.

Conclusion

No claim is allowed.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shin-Lin Chen whose telephone number is (571) 272-0726. The examiner can normally be reached on Monday to Friday from 9:30 am to 6 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for this group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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Shin-Lin Chen, Ph.D.

/Shin-Lin Chen/

Primary Examiner, Art Unit 1632